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10/584,207	11/28/2007	Terence J. Colgan	MTS5USA	3654

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/584,207	COLGAN ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,6,8-17,19-21,23-27,30-46,48 and 49* is/are pending in the application.

4a) Of the above claim(s) *11-17,23-27,30-39,43-46,48 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,6,8-10 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/10/08; 1/31/08; 10/9/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 2, 3, 4, 6, 8-10 and 19-21) in the reply filed on 17 December 2009 is acknowledged. Claims 1, 5, 7, 18, 22, 28, 29, 40-42 and 47 are cancelled.

Claims 11-17, 23-27, 30-39, 43-46, 48 and 49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 December 2009.

Claims 2, 3, 4, 6, 8-10 and 19-21 are under examination.

Claim Rejections - 35 USC § 112, first paragraph - Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4, 6, 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for endometrial cancer in a subject, the method comprising, (a) detecting the levels or amount of chaperonin 10 (CPN 10) as set forth in SEQ ID NO: 1 in an endometrial tissue sample obtained from the subject and (b) comparing the levels or amount of CPN 10 in step (a) with the levels or amount of chaperonin 10 in a control endometrial tissue

sample, wherein increased levels of CPN 10 protein expression in the sample obtained from the subject is indicative of endometrial cancer, does not reasonably provide enablement for the claims as broadly recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(i) The phrase, “endometrial disease” is broad. The specification defines endometrial disease in the following way at paragraph [0148] of the publication:

> Endometrial disease" refers to any disorder, disease, condition, syndrome or combination of manifestations or symptoms recognized or diagnosed as a disorder of the endometrium, including but not limited to hyperplasia and cancer precursors, endometrial cancer or carcinoma, endometriosis, reproductive disorders, and infertility.

Thus the term endometrial disease is defined openly and not limited to endometrial cancer, nevertheless, the examples in the specification only teach the detection of

endometrial cancer using CPN 10 as a marker. For instance, at paragraph [0439] of the publication:

> Chaperonin 10 was not identified exclusively in malignant endometrial tissues; low levels were detected in non-malignant endometrial tissues by both mass spectrometry and western blotting techniques (Table 2). Furthermore, there is no apparent association between any particular histopathologic classification and the detection of these low levels of chaperonin 10. In contrast, high levels of chaperonin 10 were detected in 17 of 22 malignant endometrial tissues by either mass spectrometry and/or western blotting techniques (Table 3). The apparent absence of chaperonin 10 in the remaining five of the 22 malignant cases may be due to either true absence or technical factors in pre-analytic processing or proteomic analysis. In two of these five cases, re-examination of the corresponding mirror image histologic section revealed minimal tumor in one case (case 28), or abundant necrosis of tumor (case 44). Furthermore, specific protein peaks of interest may be obscured in less-than-optimal mass spectromectric analysis or by adjacent protein peaks.

Similarly, the literature teaches the use of CPN 10 as a cancer marker. For instance, see Yang et al., Journal of Proteome Research, 2004; 3: 636-643—on Applicants' 1449 form and Dube et al. Journal of Proteome Research, 2007; 6: 2648-2655, both of which teach overexpression of CPN 10 protein in malignant endometrial tissue. Early pregnancy factor, which is an extracellular form of CPN 10 (see Somodevilla-Torres et al., Cell Stress & Chaperones, 2000; 5: 14-20 and Cavanaugh and Morton, Eur. J. Biochem. 1994; 222: 551-560—both on Applicants' 1449 form), can also be used to distinguish between benign from malignant trophoblastic tumor (see Xiaoguang et al., American Journal of Reproductive Immunology, 1999; 41: 204-208—on Applicants' 1449 form). Furthermore, the literature also teaches that early pregnancy factor, can be used as a marker for pregnancy, therefore it would not be an appropriate marker for "reproductive disorders and infertility," as defined in the

specification (see Example 9 of EP 0 316 919—on Applicants' 1449 form). Regarding infertility, DeSouza et al. (Proteomics, 2005; 5: 270-281—on Applicants' 1449 form) failed to show that CPN 10 was differentially expressed in the endometria from infertile women (see abstract; p. 275-277, Table 1). In short, neither the teachings of the specification nor the literature support the breadth of the recitation that CPN 10 could be used as a marker for all possible endometrial diseases.

(ii) The phrase "biological sample" is broad". The specification teaches that a biological sample can be derived from any biological source, for instance, see the publication at paragraph [0150]), which reads:

> The terms "sample", "biological sample", and the like mean a material known or suspected of expressing or containing one or more endometrial polynucleotide markers or one or more endometrial markers. A test sample can be used directly as obtained from the source or following a pretreatment to modify the character of the sample. The sample can be derived from any biological source, such as tissues, extracts, or cell cultures, including cells (e.g. tumor cells), cell lysates, and physiological fluids, such as, for example, whole blood, plasma, serum, saliva, ocular lens fluid, cerebral spinal fluid, sweat, urine, milk, ascites fluid, synovial fluid, peritoneal fluid, lavage fluid, and the like. The sample can be obtained from animals, preferably mammals, most preferably humans. The sample can be treated prior to use, such as preparing plasma from blood, diluting viscous fluids, and the like. Methods of treatment can involve filtration: distillation, extraction, concentration, inactivation of interfering components, the addition of reagents, and the like.

The specification teaches the measurement of CPN 10 protein in endometrial tissue. In spite of the limitations of using whole tissue homogenates, the specification does provide evidence that high expression levels of CPN 10 in endometrial tissue relative to control endometrial tissue is indicative of endometrial cancer. See paragraph [0438] of the publication:

> Despite the limitations of using whole tissue homogenates for protein expression profiling, this preliminary study of endometrial carcinoma has shown that proteomic analysis of endometrial carcinoma can detect differences from that of normal endometrium. Furthermore, a specific protein (Chaperonin 10) was strongly associated with endometrial carcinoma cases. This potential marker might be clinically useful on tissue aspirates since its differential expression pattern can be detected without the LCM procedure.

Since, as noted above, detection of CPN 10 in the blood can be a marker of pregnancy, measurement of CPN 10 in this sample would be non-specific. Xiaoguang et al. (cited above) teach that measurement of early pregnancy factor in the serum was an "indicator to distinguish benign from malignant trophoblastic tumor." (See whole article). Further, Yang et al. (Journal of Proteome Research, 2004; 3: 636-643—on Applicants' 1449 form) teaches at p. 637, left column, middle paragraph teaches about the trouble of using serum as a tissue and also the state of the art with respect to tissue sampling for endometrial cancer markers:

> [A]s every tissue can potentially secrete or discharge into blood, the link between a discriminating protein found in blood and the disease is tenuous until it can be established that the protein is specifically expressed in the diseased tissue. In this study, we have decided to bypass serum and analyze directly the tissue. In this first round, we used as samples homogenates of tumorous and normal endometria. As we will later show, we were able to localize the tumor marker to endometrial epithelial cells by immunohistochemistry. A potential disadvantage of using endometrial tissue as opposed to serum for analysis is that sampling is significantly more invasive. Obviously, the major advantage is the direct link between any potential marker and the endometrium. In the future, it may be possible to sample, using a technique of lower invasiveness, endometrial cells, debris, and secretions by means of a uterine lavage for proteomic analysis.

Note that the art teaches that it is still not possible to detect cancer markers such as CPN 10 using endometrial cells, debris, and secretions by means of a uterine lavage, thus "biological sample" encompasses a number of as yet non-operative embodiments.

(iii) Regarding claims 3 and 10, the specification does not teach "pre-determined" standards or "cut off values", but rather the examples teach that the relative protein levels of CPN 10 in endometrial tissue from endometrial cancer patients are higher with respect to controls. The blotting techniques used to detect relative protein levels in the specification are semi-quantitative. There is no teaching of a cut off value that has been pre-determined; Tables 2 and 3 only show measurements in terms of intensity of expression. The recitation of pre-determined standards or cut-off values would require one skilled in the art to undertake empirical research to establish those standards and values. Finally, recent work by the inventors (Yang et al. and Dube et al.—both cited above) do not teach "pre-determined" standards or "cut off values", thus the recitation of these "pre-determined" standards or "cut off values" is an invitation to the skilled artisan to undertake further research to discover these parameters.

(iv) Chaperonin 10 is defined in the specification at paragraphs [0163] in the following way:

> The term "chaperonin 10", "chaperonin 10 polypeptide" or "chaperonin protein" includes human chaperonin 10, in particular the native-sequence polypeptide, isoforms, chimeric polypeptides, all homologs, fragments, precursors, complexes, and modified forms and derivatives of human chaperonin 10.

Considering that the invention contemplates measuring chaperonin 10 levels by proteomic methods as a marker for endometrial cancer, it is important that the test be

accurate with the highest level of sensitivity and specificity. A test that can detect any isoform, chimeric polypeptide, homolog, fragment or modified form of chaperonin 10 would sacrifice a great deal in specificity. One skilled in the art would be required to undergo undue experimentation to identify those chaperonin 10 mutein measurements that accurately predict cancerous or non-cancerous endometrium.

(v) Proteomics technology is complex and unpredictable. Note the news report by Erika Check (Nature, 2004; 429: 496-497—on Applicants' 1449 form), which explains that the field has not yet had the opportunity to develop standards for interpreting test results. An illustrative example is given regarding internal inconsistencies in the data of an early detection test for ovarian cancer. The issues raised under points (i) – (iv) are exacerbated given the complexity and unpredictability of proteomics technology.

Due to the large quantity of experimentation necessary to determine which chaperonin 10 muteins can be detected in which biological samples and shown to be differentially expressed between those patients with and without endometrial disease and to therefore accurately predict said endometrial disease, and furthermore, to develop cut-off values and pre-determined standards of chaperonin 10; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention; the unpredictable state of proteomics technology and its ability to accurately predict cancer; (the level of skill of those in the art); and the breadth of the claims which fail to recite limitations on the biological sample, the disease and the chaperonin 10 mutein, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 10, 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(a) Claim 10 recites detecting “multiple cancer markers”, which is broad. The phrase is defined at paragraph [0018]:

> Endometrial markers identified in accordance with a method of the invention, (including the endometrial cancer markers listed in Table 1, 4, 5, or 6), and polynucleotides encoding the markers, have application in the determination of the status or phase of the endometrium and in the

> detection of an endometrial disease such as endometrial cancer. Thus, the markers can be used for diagnosis, monitoring (i.e. monitoring progression or therapeutic treatment), prognosis, treatment, or classification of an endometrial disease (e.g. endometrial cancer), or as markers before surgery or after relapse. The invention also contemplates methods for assessing the status of an endometrial tissue, and methods for the diagnosis and therapy of an endometrial disease.

According to the specification throughout pages 73 and 74, most of the proteins in Table 6 are not differentially expressed between normal and cancerous endometria, thus the proteins therein would not be useful as cancer markers. For instance, see paragraph [0480]:

> Table 6 lists the 119 proteins that have been identified by ProICAT and verified by manual inspection of MS/MS data. FIG. 19 shows the distributions of the proteins in the form of a pie chart. Of the 119 proteins, 15 were added after manual inspection of 50 randomly selected proteins' MS/MS spectra. If the MS/MS spectra of the remaining 151 proteins was inspected, it would have been expected to confirm the identifications of an additional .about.45 proteins. This, however, was considered impractical, especially after it was known that none of the 15 additional proteins were observed in all three runs and would contribute towards knowledge of differential expression.

And paragraph [0483], which indicates only five proteins from Table 6 were consistently identified as differentially expressed: "only five of these 24 proteins were observed in all three samples (and an additional one in two samples). All five proteins were identified by single tryptic peptides." In summary, most of the "cancer markers" as defined in the specification, represent inoperative embodiments.

(b) Proteomics technology is complex and unpredictable. Note the news report by Erika Check (Nature, 2004; 429: 496-497—on Applicants' 1449 form), which explains that the field has not yet had the opportunity to develop standards for interpreting test results. An illustrative example is given regarding internal inconsistencies in the data of

an early detection test for ovarian cancer. Given the complexity and unpredictability of the technology, Applicants are not enabled for "cancer markers", many of which are indicated in the specification as not being differentially expressed between normal and diseased endometrial tissue.

(c) The goals of claims 19-21 are to monitor the progression of endometrial cancer (claim 19), to determine a subject in which endometrial cancer has metastasized or is likely to metastasize in the future (claim 20) and to assess the aggressiveness or indolence of endometrial cancer in a subject (claim 21) comprising comparing levels or amounts of chaperonin 10 in a subject to a normal value. It is noted that the specification does not teach "pre-determined" standards or "cut off values", but rather the examples teach that the relative protein levels of CPN 10 in endometrial tissue from endometrial cancer patients are higher with respect to controls. Further, paragraph [0439] teaches that 5/22 or 23% of cancer subjects had undetectable levels of CPN 10, thus indicating that the current test does not even detect CPN 10 in all of the possible cases. Furthermore, the techniques used to detect relative protein levels in the specification are semi-quantitative. There is no teaching that a cut off value that has been pre-determined, which would be required if one was to use the tests not merely to screen for the possibility of endometrial cancer, but also to monitor its progression. Tables 2 and 3 only show measurements in terms of intensity of expression. The specification does not provide a nexus between these protein measurements and the stage of endometrial cancer, cancer aggressiveness, or whether the cancer has or will metastasize. The need for pre-determined standards or cut-off values for the more

detailed methods of monitoring progression of the disease require one skilled in the art to undertake empirical research to establish those standards and values. Finally, recent work by the inventors (Yang et al. and Dube et al.—both cited above) do not teach the existence of pre-determined standards or cut off values that would enable one skilled in the art to undertake the more detailed methods of monitoring progression of endometiral disease. The methods recited in claims 19-21 represent an invitation to the skilled artisan to undertake further research to discover the parameters needed to carry out the goals of the methods.

(d) Furthermore, even if Applicants were enabled for claims 10 and 19-21, the issue raised in the preceding rejection under 35 U.S.C. 112, first paragraph over claims 2-4, 6, 8 and 9 (points (i) – (v)) above are also applicable here and are hereby incorporated.

Due to the large quantity of experimentation necessary to determine values of chaperonin 10 that would be capable of monitoring progression of disease as recited in the claims, which cancer markers can be detected that are differentially expressed between those patients with and without endometrial disease to therefore accurately predict said endometrial disease, and which biological samples can be used to carry out the methods; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention; the unpredictable state of proteomics technology and its ability to accurately predict cancer, (the level of skill of those in the art); and the breadth of the claims which fail to recite limitations on the biological sample, the disease, the

chaperonin 10 mutein and the cancer markers, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Xiaoguang et al. (AJRI, 1999; 41: 204-208—on Applicants' 1449 form). The claims are drawn to a method of screening for an endometrial disease in a subject, the method comprising: (a) detecting the level or amount of chaperonin 10 in a biological sample obtained from the subject, wherein the biological sample is obtained from a tissue, extract, cell culture, cell lysate, lavage fluid or physiological fluid (claim 8); and (b) comparing the level or amount in step (a) with a level or amount of chaperonin 10 in a control, wherein a significant difference in the levels or amount of chaperonin 10 in the biological sample, relative to the corresponding level or amount in the control, is indicative of endometrial disease (claim 2) and a method as claimed in claim 2, further comprising: (a) contacting the biological sample obtained from a subject with at least one binding agent that specifically binds to chaperonin 10; and (b) detecting in the biological sample the level or amounts of chaperonin 10 that binds to the binding agents, relative to a pre-determined standard or cut-off value, and therefrom determining the presence or absence of the endometrial disease in the subject (claim 3), wherein the binding agent is an antibody (claim 4).

Xiaoguang et al. teach the assaying of the activity of early pregnancy factor or EPF, which is highly homologous to chaperonin 10 (p. 204; first sentence) in order to determine malignant trophoblastic tumor. The activity is measurement by the rosette inhibition titer or RIT. Note that detecting is broadly defined in the specification at paragraph [0031]:

The term "detect" or "detecting" includes assaying, imaging or otherwise establishing the presence or absence of the target endometrial markers or polynucleotides encoding

the markers, subunits thereof, or combinations of reagent bound targets, and the like, or assaying for, imaging, ascertaining, establishing, or otherwise determining one or more factual characteristics of an endometrium phase or endometrial disease including cancer, metastasis, stage, or similar conditions. The term encompasses diagnostic, prognostic, and monitoring applications for the endometrial markers and polynucleotides encoding the markers.

Since detecting is defined as encompassing assaying, this limitation is met. Since the RIT employs a pre-determined standard as described at p. 205, right column, under "Rosette Inhibition Assay," in which "pre-chemotherapy patients reached a higher RIT value" (see p. 206), the limitation of claim 3 is met. Since the RIT employs the use of antilylmphocyte serum, this meets the limitation of claim 4. "Endometrial disease is defined very broadly at paragraph [0148] of the instant specification:

> Endometrial disease" refers to any disorder, disease, condition, syndrome or combination of manifestations or symptoms recognized or diagnosed as a disorder of the endometrium, including but not limited to hyperplasia and cancer precursors, endometrial cancer or carcinoma, endometriosis, reproductive disorders, and infertility.

Thus the term "endometrial disease" is defined openly and not limited to endometrial cancer. Finally, since sera is used, this meets the limitation of physiological fluids of claim 8. Thus the claims cannot be distinguished from the prior art.

Claims 2-4, 8 and 9 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Warrington et al., 2001/0044104, published 22 November 2001 in view of zellnet.com/nss-folder/pictures/Fig1.gif, downloaded 8 March 2010.

As noted above, the claims are drawn to a method of screening for an endometrial disease in a subject, the method comprising: (a) detecting the level or

amount of chaperonin 10 in a biological sample obtained from the subject, wherein the biological sample is obtained from a tissue, extract, cell culture, cell lysate, lavage fluid or physiological fluid (claim 8); and (b) comparing the level or amount in step (a) with a level or amount of chaperonin 10 in a control, wherein a significant difference in the levels or amount of chaperonin 10 in the biological sample, relative to the corresponding level or amount in the control, is indicative of endometrial disease (claim 2) and a method as claimed in claim 2, further comprising: (a) contacting the biological sample obtained from a subject with at least one binding agent that specifically binds to chaperonin 10; and (b) detecting in the biological sample the level or amounts of chaperonin 10 that binds to the binding agents, relative to a pre-determined standard or cut-off value, and therefrom determining the presence or absence of the endometrial disease in the subject (claim 3), wherein the binding agent is an antibody (claim 4).

Warrington et al. teach the use of peptide arrays to measure peptide expression profiles at paragraph [0011] and a description of "expression profiles", including measurement of "peptide abundances" is described at paragraph [0026]. Thus Warrington et al. teach an alternative embodiment of measuring peptides, or in the alternative, suggest to one of ordinary skill in the art that this could be done in lieu of mRNA or cDNA. Peptide arrays use antibodies and this is shown by the website: zellnet.com/nss-folder/pictures/Fig1.gif, which is a schematic of a peptide array. Paragraphs [0034], [0057], [0073] and claim 1 of Warrington et al. teach comparing expression levels of proteins in diagnosing disease states and paragraph [0052] lists endometrial cancer, thus suggesting to one of skill in the art that peptide expression

levels can be used as a diagnostic tool. Table 6 indicates chaperonin 10 is one of the genes that is differentially expressed at least four-fold in endometrial cancer, thus teaching the measurement in tumor tissue (claims 8 and 9). It is noted that Warrington et al. indicate that translation state relates to "the relative abundances of the constituent protein species in the sample," and further goes on to teach that transcriptional and translational states are related (i.e., protein levels are related to gene expression) (paragraph [0030]), thus strongly suggesting to one of ordinary skill in the art that measuring peptide expression levels is strongly related to gene expression levels. In conclusion, Warrington et al. teach the measurement of protein, its relationship to RNA levels, and the differential expression of the chaperonin 10 gene in endometrial cancer, thus suggesting that chaperonin 10 is a marker of tumorigenic vs. normal endometria. In short, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to measure protein expression levels in lieu of gene expression levels because Warrington et al. teach that one can be substituted for the other since transcriptional and translational states are related (i.e., protein levels are related to gene expression) (paragraph [0030]). The person of ordinary skill in the art would have been motivated to measure peptide levels because it represents the simple substitution of one known, equivalent element for another to obtain predictable results. Thus the claims do not contribute anything non-obvious over the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest

/Bridget E Bunner/
Primary Examiner, Art Unit 1647